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Invited Review Article

# Dietary Boron : Possible Roles in Human and Animal Physiology#

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**Abstract**

Boron is a bioactive element of low molecular weight. Since discovery of the first boron biomolecule, boromycin, in 1967, several other similar biomolecules are now well-characterized. Most recently described was a bacterial cell-to-cell communication signal that requires boron. Boron is a natural constituent of the diet and human consumption is not trivial : ~1.00 mg/d for males aged 51 to 70 y. Boron may be under homeostatic control in humans and other mammals through regulatory mechanisms that remain undefined. Evidence for such control is enhanced by discovery of a specific mammalian borate transporter, NaBC1, expressed in the basolateral membranes of epithelial cells in tissues with excretory functions including kidney. Gastrointestinal absorption of boron approaches 100% but, even so, boron has a low order of toxicity. For adults, the Tolerable Upper Intake Level (UL) for boron is 20 mg/d, i.e., ~20-fold typical intakes. The Institute of Medicine has not set an Estimated Average Requirement (EAR), Recommended Dietary Allowance (RDA), or Adequate Intake (AI) for boron because the collective body of evidence has yet to establish a clear biological function for boron in humans. The evidence to date suggests that humans and higher animals (frog, zebrafish, chick, rat, and pig) may use boron to support normal biological functions. These findings suggest that boron has a role in bone structure and function, inflammation and immune processes, insulin metabolism, and completion of the life cycle. Development of animal models that lack boron transporters may help in identification of mechanisms of action responsible for the beneficial effects of dietary boron.

Keywords : boron nutrition and, inflammation, bone and mineral metabolism, insulin metabolism

## 1. Introduction

The importance of boron in biology was first recognized over 80 years ago with the discovery that boron is essential for the completion of the life cycle in higher plants in phylogenetic kingdom Viridiplantae [1, 2]. More recently, boron was recognized as required for at least some organisms in Eubacteria [3], Protista [4], and Animalia [5, 6]. Specific species in the Fungi kingdom have a demonstrated physiological response to boron [7], an important finding because Fungi species are thought to share a common ancestor with animals exclusive of plants [8]. This review summarizes present understanding regarding the biological actions of boron in human physiology and health.

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## 2. BORON BIOCHEMISTRY

### 2.1. Boron speciation in biological systems

Boron is a bioactive element of low molecular weight (atomic weight = 10.81 $g \cdot mol^{-1}$). Within the intestinal tract, most ingested boron is probably converted to inorganic orthoboric acid (common name : boric acid) B

$(OH)_3$, the normal end product of hydrolysis of most boron compounds [9]. Boric acid is not a proton donor, but instead, accepts a hydroxyl ion (a Lewis acid) to form the tetrahedral anion $B(OH)_4^-$ (Reaction 1) [10] :

$$B(OH)_3 + 2H_2O \leftrightarrow H_3O^+ + B(OH)_4^- \quad pK_a = 9.25\ (25℃) \quad (1)$$

At physiological concentrations (0.006 - ~9.0 μmol/L), inorganic boron is essentially present only as $B(OH)_3$ and $B(OH)_4^-$ [11]. Within the normal pH range of the gut and kidney, $B(OH)_3$ prevails as the dominant species (pH 1 : ~100% $B(OH)_3$ ; pH 9.3 : 50% ; pH 11 : ~0%) [12]. Uptake of boron from diets naturally low in boron as well as uptake from supplemental dietary inorganic forms approaches 100% [13].

## 2.2. Boron esters and complexes

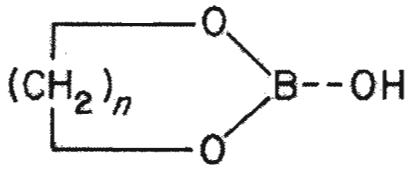
The unique nature of boron allows the element to form complexes with a vast number of biomolecules under normal physiological conditions. For example, the boroesters are chemical structures formed by reactions between B-O compounds and certain mono or polyhydroxy compounds to form specific B-containing complexes. Boroesters probably represent the most biologically relevant B species because of the vast number of biochemicals that contain one or more hydroxyl groups with suitable positions. Boric acid reacts with suitable dihydroxy compounds to form the corresponding boric acid monoesters ("partial" esterification) (e.g., Structure 1) that retain the trigonal-planar configuration and no charge. The reaction that produces boromonoesters is easily reversible ; the ester is completely hydrolyzed when transferred into water. Because boromonoesters are easily hydrolyzed when placed in aqueous solutions, it seems reasonable that boromonoesters may be isolated from hydrophobic environments (e.g., the lipid portions of the plasmalemma) where the absence of water shifts the equilibrium to the right (reaction 2) [10].

$$B(OH)_3 + 3ROH \Leftrightarrow B(OR)_3 + 3H_2O \quad (2)$$

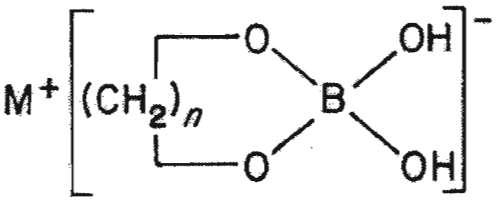
A borate monoester with a tetrahedral configuration and a negative charge (Structure 2) is created when borate forms a complex with a suitable dihydroxy compound. A compound of similar configuration and charge is also formed when a boric acid monoester forms a complex with an available hydroxyl group. These two types of boromonoesters can react with another dihydroxy compound to give a corresponding spiro-cyclic borodiester ("complete" esterification) that is a chelate complex characterized by a central B atom coordinated by four O atoms in a tetrahedral configuration and negative charge (Structure 3) [14]. Substances carrying two cis-hydroxyl groups on adjacent carbons form very stable diester complexes (Structure 3 [15], which are almost undissociable in water [16]. The greater stability of borodiesters, compared to boromonoesters, probably explains why the known B-containing biomolecules described later are characterized by a B atom bound to four oxy groups.

### 2.2.1. Nucleotide-boron adduction

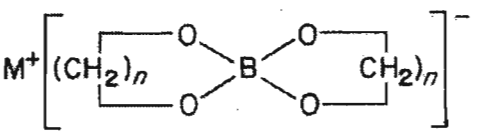
Ribose derivatives have a strong affinity for boron [17] and nucleotide-boron adduction has been demonstrated for a number of ribose-containing nucleotides and




**Structure 1**

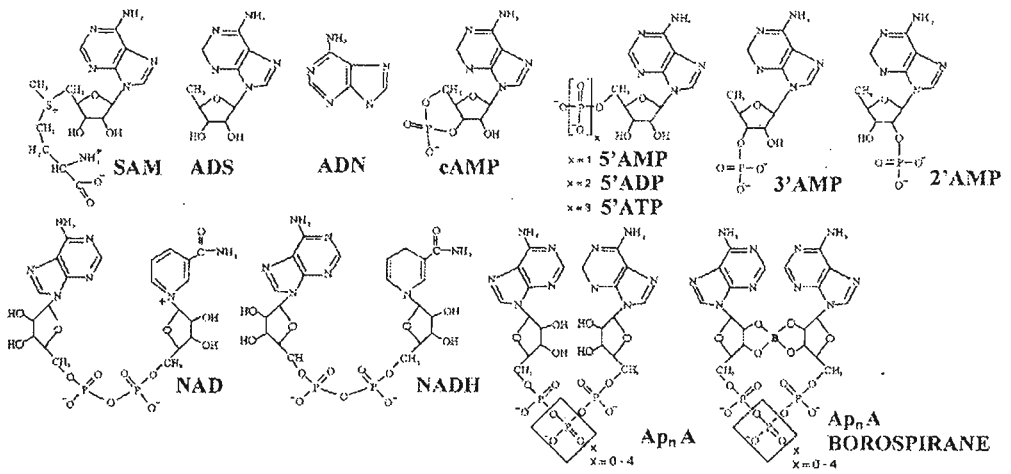



**Structure 2**




**Structure 3**

cofactors, all with different affinities for boron (Structure 4) [18]. S-adenosylmethionine (SAM) (**Structure 4**) is the predominant methyl donor in biological methylations and is therefore a versatile cofactor in a variety of physiologic processes [19]. It was demonstrated that SAM has a far greater affinity for boron than do several other tested monoadenosine species : SAM>>5'ATP>5'ADP>5'AMP>adenosine (ADS) ≅ 3'AMP ≅ 2'AMP ≅ cAMP ≅ adenine (ADN) [18]. The rank order of boron binding to these various species indicates that boron binding by the 2'-3'-cis-diols of the ribose moiety of SAM was electrostatically stabilized by the cationic sul-




**Structure 4**

fur of the methionine and interaction with the terminal amino and carboxyl groups on its methionine. Boron does not bind to either ADN or cAMP because of the lack of ribose or absence of an intact ribose binding site on these respective species.

The pyridine (e.g., $NAD^+$ or NADP) and flavin (e.g., FAD) nucleotides (**Structure 4**) are essential co-factors for five sub-subclasses of oxidoreductase enzymes. These co-factors have received special attention as they contain a ribose moiety with a cisoid diol conformation [20] that interacts with boron to cause reversible in vitro inhibition of the oxidoreductases that require pyridine or flavin nucleotides. Until recently, $NAD^+$ ($K_d$ of 14.4 mM) was recognized as having the highest boron binding affinity of any biomolecule that occurs naturally in animals. Borate interacts with $NAD^+$ to form an anionic complex where $NAD^+$ is electrostatically stabilized by the cationic nitrogen of the nicotinamide of $NAD^+$ (Kd 14.4 mM), a charge that is not present on NADH (Kd 26.4 mM) [21]. This need for electrostatic stabilization also has the probable functional consequence of limiting, at physiological concentrations, the reaction of boron with many ribosyl-containing compounds including most, if not all other, nucleotides.

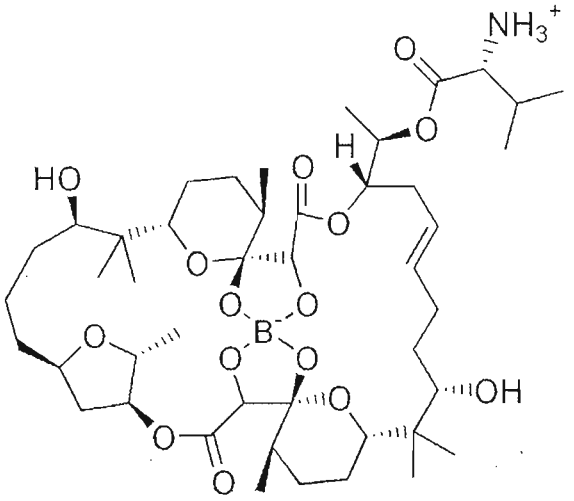
Structurally similar to $NAD^+$ and NADH, the di-adenosine-phosphates ($Ap_nA$) all possess a pair of ribose moieties held in close proximity, joined by 2-6 phosphodiesters (**Structure 4**). Present in all cells with active protein synthesis, $Ap_nA$ molecules function as signal nucleotides associated with platelet aggregation and neuronal response. The $Ap_nA$ are putative "alarmones" which reportedly regulate cell proliferation, stress response, and DNA repair [22]. At physiologic pH, the adenine moieties of either Ap2A or Ap3A are driven together by hydrophobic forces and stack interfacially [21]. This stacking of the base adenines prohibits formation of a dicomplex (to resemble **Structure 3**) and, as current findings indicate [18], only allows for simple additive binding between boron and two independent monocomplexes. However, for $Ap_nA$ with four or more intervening phosphates, boron binding apparently is cooperative, i.e., the adenosine bases do not stack and a unimolecular dicomplex binding of boron occurs between the vicinal cis-hydroxyls of the opposing ribose moieties (Structure 4 ; $Ap_nA$ borospirane). Thus, boron binding by $Ap_4A$, $Ap_5A$ and $Ap_6A$ is greatly enhanced compared $Ap_3A$ or $Ap_2A$, $NAD^+$, NADH or any of the tested mono-adenosines except for SAM. In summary, there is strong evidence that SAM and certain $Ap_nA$ families bind boron with higher affinities than does $NAD^+$, formerly recognized as the highest affinity boron ligand present in animals.

### 2.2.1 Boron-Containing Biomolecules

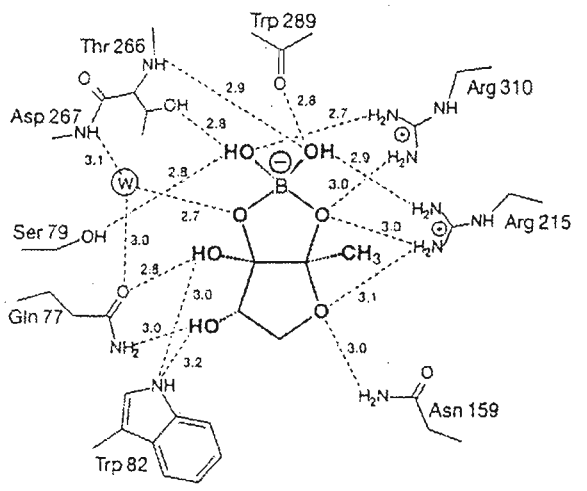
The discovery of all currently recognized boron-dependent biomolecules was achieved because the bound boron formed four coordinate covalent bonds with the ligand, creating a thermodynamically stable complex that is almost undissociable in water [16, 23].

Boromycin was the first boron biomolecule to be discovered (Structure 5). It is an antibiotic produced by a strain of Streptomyces antibioticus [24] and conforms to the chemical structure characteristic of a boroester. Recently, boromycin, was discovered [25] to be a potent anti-human immunonodeficiency virus (HIV) antibiotic. It strongly inhibits the replication of the clinically isolated HIV-1 strain and apparently blocks release of infectious HIV particles from cells chronically infected with HIV-1 by unknown mechanisms.

Several other similar boron biomolecules are now well-characterized [17, 26, 27]. Most recently described



**Structure 5** Boromycin



**Structure 6** LuxP-AI-2 complex [28]

was the bacterial molecule, autoinducer-2 (AI-2), a cell-to-cell communication signal that requires boron [28]. This biomolecule is produced by a large number of bacterial species and synthesis begins with the common metabolite, S-adenosylmethionine (SAM) (Pathway 1). Intermediate metabolites include S-ribosylhomocysteine which contributes a ribose moiety. Further enzymatic modification yields a precursor that reacts with borate to form AI-2, a classical borate monoester. AI-2 binds to the primary receptor, LuxP, to form a furanosyl borate diester complex (Structure 6). In the bioluminescent marine bacterium *V. harveyi,* AI-2 signalling stimulates light production and boric acid concentrations as low as 10 μM causes a tenfold induction in bioluminescence [28].

Based on the structure of known boron-containing biomolecules, it is reasonable to predict that several biomolecules waiting discovery are derived from ribose and serve as signaling molecules that interact with the cell surface. Because known boron biomolecules are comprised of mirror or near-mirror halves stabilized by a single boron atom, it is predicted that undiscovered biomolecules have similar mirror construction.

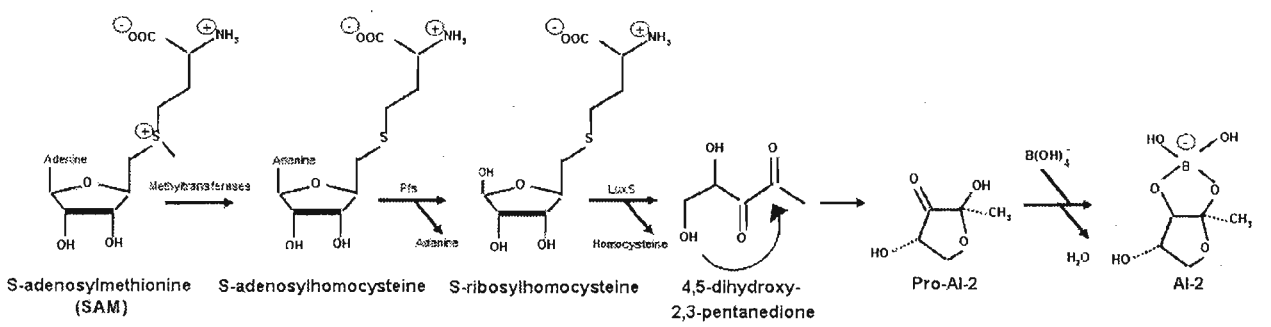
## 3. BORON CONCENTRATIONS IN HEALTHY TISSUES

Boron is present at comparable concentrations in healthy tissues of different animals. Similar concentrations of boron (μg/ml) were reported in the plasma of humans (0.017-0.191) [13, 29-34], rats (0.038-0.039) [35], chicks (0.047-0.152) [36], cows (0.052-0.153) [37], lambs (0.163) [36], pigs (0.126) [36], and horses (0.227) [36]. When expressed on a molar basis, plasma boron concentrations in humans (0.002-0.018 μmol/ml) [13, 29-34], are similar to those of the trace elements zinc (0.011-0.018 μmol/ml), iron (0.011-0.032 μmol/ml), and copper (0.011-0.022 μmol/ml) [38]. Liver boron concentrations (μg/g ; dry weight) are similar in humans (1.1-5.4) [39, 40], rats (0.51) [41], chicks (1.01-4.4) [42], and cows (3.3) [40] ; for brain tissue (μg/g ; dry weight), similar in humans (0.87) [39], rats (0.64) [41], and chicks (1.01-1.05) ; for bone tissue (μg/g ; dry weight), similar in humans (1.6) [29], rats (1.3-1.7) [41, 43], chicks (0.59-0.64) [44], and mule deer (1.7) [45].

## 4. ENVIRONMENTAL BORON

### 4.1 Dietary Intakes of Boron

Boron is ubiquitous in the environment and, on a mo-




**Pathway 1** Biosynthesis of AI-2.

lar basis, adult Americans consume more boron than several essential trace elements, e.g., copper, manganese, and molybdenum [46]. Boron consumption apparently varies considerably among individuals and by sex-age group. For example, boron intake for infants aged 0 to 6 months was estimated to be 0.75±0.14 mg/d (mean±SE) ($1^{st}$ percentile, 0.03 ; $99^{th}$ percentile, 6.40 mg/d) ; for males aged 51 to 70 years, 1.34±0.02 mg/d ($1^{st}$ percentile, 0.39 ; $99^{th}$ percentile, 3.34 mg/d) ; for lactating females, 1.39±0.16 mg/d ($1^{st}$ percentile, 0.38 ; $99^{th}$ percentile, 3.49 mg/d) [47]. In China, the mean dietary boron intake for adult males was estimated to be 1.27 mg/d [48].

The range of dietary boron intakes within a sex-age group may arise from a variety of factors. For example, compared with animal-based food products, plant-based products are much richer sources of dietary boron [46]. Furthermore, most plant species within the subclass Dicotyledoneae, which includes fruits [i.e., raw pears : 2.27 μg (0.21 μmol) B/g], vegetables, tubers and legumes have much higher concentrations of boron than do species from the subclass Monocotyledoneae, especially gramineaceous species (the grasses) including rice [0.09 μg (0.008 μmol) B/g], corn, barley, and wheat [46]. For this reason, there are many diets that provide only 0.36 mg B/2000 Kcal (and otherwise nutritionally adequate) and are prepared easily by excluding vegetables, tubers, nuts, legumes, and fruits (good sources of boron) [13]. Water is an extremely variable source of boron. For example, boron concentrations in the tap water from Iskele and Balikesir, two villages in Turkey separated by only 50 km, are 2 mg/l and <0.20 mg/l respectively. Boron intakes (calculated by urinary excretion) of adult males living in these respective villages differ substantially : 6.8 mg/d versus 1.3 mg/d [49].

### 4.2 Boron Toxicity

Boron has a low order of toxicity. The Institute of Medicine has established a boron intake of 20 mg/d as the Tolerable Upper Intake Level (UL) for adults [47], a value 20-fold higher than typical intakes. Boron can be toxic in all tested biological organisms at excessive amounts but mechanisms of action are not well elucidated. Boric acid complexes with the polyhydroxyl ribitol side chain of riboflavin to greatly increase the water solubility of riboflavin and individuals who have consumed large amounts of boric acid or its derivatives (either accidentally or with suicidal intent) excrete high levels of riboflavin within the first 24 to 48 hours following ingestion [50]. Boron dose response experiments to determine embryo-larval malformations in the rainbow trout, *Oncorhyncus mykiss* [51], and frog, *Xenopus laevis* [6], and have demonstrated the pattern of survival, deficiency, optimization, toxicity, and lethality similar to the essential elements zinc and copper. However, boron produced a much wider concentration-response curve for teratogenesis than either copper zinc in Xenopus, indicating a wider margin of safety for boron, compared to zinc or copper, between nutritionally deficient levels and the greater toxic levels [6].

The minimum lethal dose of ingested boric acid (17.5% B) has not been determined precisely but has been estimated to be 2-3 g in infants and 5-6 g in children [52]. Death occurred in a 66 yr old man after accidental ingestion of 45 g of borax (11.3% boron) [53], but data from a retrospective chart review of 784 cases indicate that ingestions of up to 88.8 g of boric acid caused minimal or no manifestations of boron toxicity in patients ≥ 6 yr of age [54]. Adults have survived single intakes of ~300 g of boric acid [55].

## 5. EVIDENCE FOR BORON HOMEOSTATIC MECHANISMS

There are several lines of evidence suggesting that boron may be homeostatically regulated in humans. That boron contents in human milks were similar and stable throughout lactation of full term infants in two cohorts of women living in either Houston, TX, [56] or St. John's, Newfoundland (Figure 1) [57] may suggest regulatory mechanisms for the element, which remain undefined.

Substantial increases in dietary boron in elderly women [0.3 mg/d ($1^{st}$ percentile of typical intake) to 3.0

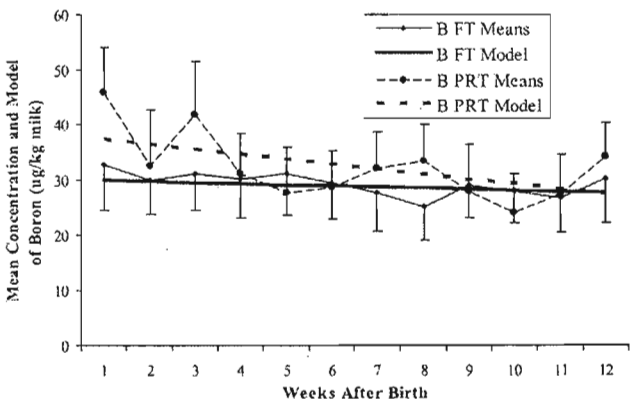



**Fig. 1** Model and mean (±SE) concentrations of boron in breast milk from mothers of full-term (FT) and premature (PRT) infants living in St. John's, Newfoundland, Canada ; n = 9 per group over the 12 wk after birth. During the first 12 wk of lactation, prematurity affected the rate of change in concentrations (P = 0.01) [57].

mg/d (~99$^{th}$ percentile of typical intake)] resulted in only small changes in blood boron values [13]. Other investigators have also reported a remarkably narrow range of boron concentrations in whole blood from subjects with unknown dietary histories [58]. Likewise, chicks fed a 9-fold increase in dietary boron, compared to those fed a low-boron diet, exhibited only a 2-fold increase in plasma boron concentration and no increase in femoral boron concentration [59].

In female rats, supplementation with high amounts of boron (9.25 mmol/L water) for 21 days, caused an increase in plasma boron concentrations but an undefined homeostatic mechanism concurrently eliminated any excess of boron from the liver and brain against their own concentration gradients [60]. In yearling beef heifers, total urine weight did not change significantly with increased boron intake but the percent of filtered boron reabsorbed by the kidneys decreased significantly with increased boron intake [61]. In general, the findings to present suggest the presence of boron concentration against a gradient across mammalian cell membranes. Cultures of either RAW 264.7 cells or HL60 cells retain intracellular boron against a concentration gradient indicated the presence of intracellular boron binding species or the existence of boron specific transporters on the plasma membrane [62].

Most likely, the repeated demonstration of the concentration of boron against a gradient indicates the existence of boron specific transporters. This line of evidence for the homeostatic control of boron is enhanced further by the discovery of specific boron-specific transporters in plants and animals. BOR1 (AtBor1) is a boron transporter in the flowering plant, *Arabidopsis thaliana,* and mediates boron export from pericycle cells into the root stellar apoplasm against a concentration gradient [63, 64]. Cloning identified BOR1 as a membrane protein with homology to members of the bicarbonate transporter superfamily in animals [63]. Human BTR1 is a member of this superfamily [65] and it was renamed NaBC1 following the discovery that it is a $Na^+$-dependent borate transporter [66]. That is, NaBC1 acts as an electrogenic, voltage-regulated, $Na^+$-coupled $B(OH)_4^-$ transporter in the presence of borate. It shows apparent high specificity for boron and knockdown of NaBC1 nearly eliminated cell growth and proliferation in HeLa cells [66].

NaBC1 protein has been identified in epithelial cells in rat kidney, parotid gland, submandibular gland (SMG), pancreas, and liver [66]. In particular, the protein was found to be expressed in the basolateral membrane of rat SMG and kidney tubules. Importantly, SMG acinar cells, compared to duct cells, expressed a much higher level of NaBC1. The high selectivity for $Na^+$, a tight coupling of $Na^+$-$B(OH)_4^-$ cotransport, minimal $Na^+$ and $B(OH)_4^-$ leak in the presence of borate, and lack of $H^+$ and $OH^-$ transport are important properties for $B(OH)_4^-$ uptake from a low $B(OH)_4^-$ concentration. Thus, low leak, high selectivity, and coupling stoichiometry makes NaBC1 ideal as a boron-concentrating transporter [66].

## 6. BORON DEPLETION AND THE LIFE CYCLE

The original finding [67] that boron deprivation can impair growth has been the basis for further research in several independent laboratories. In the zebrafish, boron appears to be required for cell cleavage post-fertilization. For example, sperm from low-boron zebrafish males successfully fertilized eggs from low-boron females [68], but 92% of the embryos (compared to 37% of controls) died within 10 days. However, the low-boron embryos could be rescued from death if repleted with boron during the first hour after fertilization. Boron also promotes embryonic trout growth [69].

Studies with the South African clawed frog, *Xenopus laevis* [6], indicate that specimens fed a low-boron diet in a low-boron culture media produced a substantially higher number of necrotic eggs and fertilized embryos than frogs fed a boron-sufficient diet. By 96 hours of development, none of the larvae from boron-deficient adults maintained in low-boron culture media developed normally. Similar findings were reported for rats in which a low-boron diet (0.04 μg/g) reduced the number of implantation sites compared to a diet supplemented with boron [70].

## 7. BORON DEPLETION AND PHYSIOLOGICAL/ STRUCTURAL ABNORMALITIES

Several lines of evidence indicate the boron deprivation can impair bone metabolism, immunity, carcinogenesis, and glucose regulation in animals and humans.

### 7.1 Boron and Calcium Metabolism and Bone Growth and Maintenance

Observations in human studies suggest that boron can influence calcium metabolism. For example, an increase in boron intake (0.36 to 3.23 mg/d) by postmenopausal women resulted in a 5% increase in urinary calcium excretion [13]. Because increases in dietary calcium often result in increased urinary calcium excretion, this finding may reflect an increase in intestinal calcium absorption. Thus, it is important to determine whether the primary

effect of boron on calcium metabolism is at the level of enteric absorption.

Bone calcification and metabolism have been show to respond to boron nutrition. Maturation of the growth plate was retarded during dietary boron deprivation in the chick [59]. Boron deprivation reduced bone strength in pigs [71] and rats [72], and induced abnormal limb development in frogs [73]. In other studies, a boron supplement increased bone strength in nutritionally adequate chicks [74] and adult rats [75]. Recently, it was shown that boron deficiency in rats results in altered bone healing because of a marked reduction in osteogenesis [76]. In addition, boron deficiency in mice impaired periodontal alveolar bone modelling and remodelling by inhibiting bone formation [77].

Evidence suggests that dietary boron can alleviate the signs of marginal vitamin D deficiency. Marginal vitamin D deficiency is known to elevate plasma alkaline phosphatase concentration, reduce body weight, and impair bone structure. In the growing rachitic chick, dietary boron reduced elevated serum concentrations of alkaline phosphatase [67, 78], improved body weight [78, 79], and substantially alleviated the perturbed histomorphometric indices of bone growth cartilage [59, 80]. Supplemental boron was reported [79] to increase circulating 25-hydroxycholecalciferol in the marginal vitamin D deficient chick but it remains to be determined whether boron directly affects vitamin D metabolism.

### 7.2 Dietary Boron and Immune Function

Inflammation is an essential component of the host defense system, but inflammatory diseases arise from excessive inflammation. There is emerging evidence that boron supports immune function. In the only reported controlled human study for examination of dietary boron and inflammation interactions [81], twenty patients presenting radiographically confirmed osteoarthritis received either daily 6 mg (0.55 mmol) of boron (as sodium tetraborate decahydrate [borax]) as oral supplements or a placebo for 8 weeks in a double-blind trial. The arthritic individuals who received boron supplements self-reported substantial improvement in subjective measures of their arthritic condition (joint swelling, restricted movement).

The results of various animal studies have suggested a role for boron in immune function. For example, physiological amounts of dietary boron were found to have immunomodulatory effects such as reduced paw swelling and circulating neutrophil concentrations, and increased circulating concentrations of natural killer cells and CD8 $a+/CD_4^-$ (T suppressor) cells in rats with antigen-induced arthritis [82]. Pigs supplemented with boron exhibited a significant reduction in localized inflammation following administration of phytohemagglutinin [83]. Studies with pigs indicate that dietary boron supplementation increased the production of cytokines following an immune stress (lipopolysaccaride injection) [84]. Lower serum tumor necrosis factor-α and interferon-γ concentrations were observed after lipopolysaccharide injection in pigs fed a marginal boron-deficient diet than in pigs supplemented with 5 mg boron/kg diet [84]. The results indicate a definite role for physiological amounts of dietary boron in normal immune function.

### 7.3 Dietary Boron and Cancer Prevention

Boron intake has been associated with the prevalence of some cancers. More consumption of boron through drinking water was associated with a decreased incidence of cervical cancer-related histopathological findings in a population of Turkish women [85]. Analysis of data from the third National Health and Nutrition Examination Survey (NHANES III) indicate that low dietary boron intake is associated with increased prostate cancer risk [86]. Increased amounts of boron consumed as a constituent of foods strengthened the apparent protective effect of boron. Analysis of data from 763 women diagnosed with lung cancer and 838 matched healthy controls suggested an inverse association between boron intake and lung cancer [87]. As with all epidemiological-based studies, these findings are vulnerable to artifact and animal studies are needed to confirm the findings and elucidate possible mechanisms of action.

### 7.4 Dietary Boron and Insulin Metabolism

It is possible that dietary boron may reduce the amount of insulin needed to maintain glucose levels, thus limiting β-cell deterioration. For example, as a dietary ingredient, boron decreased peak pancreatic in situ insulin release in chicks (Figure 2). In rats, dietary boron decreased plasma insulin concentrations but did not change glucose concentrations [88]. These results suggest it is important to determine whether dietary boron can reduce β-cell "exhaustion" and deterioration.

## 8. CONCLUSIONS

Boron is a natural constituent of the diet and reacts with biological material or forms chelates. It is present in healthy tissues of different animals at comparable con-

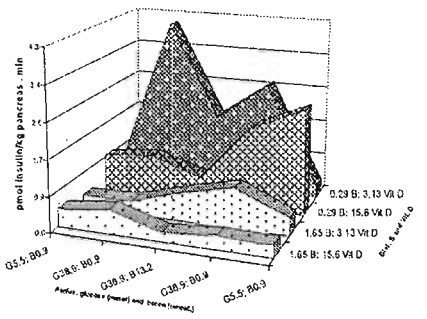


**Fig. 2** Alteration in peak insulin secretion from isolated, perfused pancreata from 1-d-old cockerels fed a diet containing 0.29 (boron-low) or 1.65 mg B/kg and supplemented with cholecalciferol (Vit D) at 3.13 (inadequate) or 15.60 (adequate) μg/kg for 26-37 d. Perfusion phases varied in the total amount of glucose (G : 5.5 or 38.0 mmol/L) and boron (B ; 0.9 or 13.2 μmol/L) in the perfusate.

centrations and toxicity results only at relatively high intakes. Tissue concentrations during short term variations in intake apparently are maintained by homeostatic mechanisms. Depletion prevents growth and completion of the life cycle in several animal species. Furthermore, depletion results in reductions of several physiologically important functions. However, the biochemical mechanisms responsible for these effects are poorly understood. Development of animal models that lack boron transporters may help in identification of mechanisms of action responsible for the beneficial effects of dietary boron. Confirmation of boron as an essential element for humans awaits identification of a human boron biomolecule that is required for performance of a vital function.

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